MAST CELL FUNCTION ASSOCIATED ANTIGEN (MAFA) PHARMACEUTICAL COMPOSITIONS AND METHODS OF MAKING AND USING THEM TECHNICAL FIELD

This application claims priority to Provisional Application Serial No. 60/190,716, filed March 17, 2000.

This invention generally pertains to the fields of cell biology, immunology and medicine. In particular, this invention provides pharmaceutical compositions and methods for controlling and modifying Natural Killer (NK) cell and T cell functions by manipulation of "mast cell function-associated antigen," or "MAFA," polypeptide-mediated cell signaling and ligand binding.

BACKGROUND

Current approaches to immune therapy for cancer and infectious diseases are limited. Several biological mechanisms may account for the inability to achieve adequate immune protection. It has been postulated that the inhibition of the cytotoxic function of anti-tumor cells, such as NK cells or T cells, by their target cells (e.g., tumor cells) may play a role in this inability. The discovery of new methods and pharmaceuticals capable of allowing the body to bypass or to block this target (tumor)-cell mediated immune inhibition would provide an important new ways to treat cancer and other diseases and conditions.

In contrast, activation of NK cell or T cell cytotoxic function can be a major obstacle to the success of allogenic transplantations, including graft and organ transplants. Activation of these cells may have a pathological role in autoimmune diseases as well. Thus, the discovery of new methods and pharmaceuticals to negatively regulate the cytolytic activity of NK or T cells would provide important means to ameliorate or block these unwanted responses by the immune system.

"Mast cell function-associated antigen," or "MAFA," was originally identified using a monoclonal antibody that inhibited rat mast cell activation in the presence of IgE. Cross-linking of cell surface MAFA inhibited IgE-stimulated mast cell degranulation (see, e.g., Ortega (1988) J. Immunol. 141:4324-4332). Cloning of the rat MAFA gene identified a type II membrane glycoprotein expressed on the surface of basophilic mast cells (see, e.g., Guthmann

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